CLAIMS

We claim:

1. A pharmaceutical agent for treating an amyloid disease in a patient, wherein the pharmacological agent comprises a therapeutically effective amount of plant matter from a plant of the genus Uncaria.

2. The pharmacological agent of claim 1 comprising a therapeutically effective amount of plant matter from a plant of the genus Uncaria, species tomentosa.

3. The pharmacological agent of claim 2 wherein the plant matter comprises an extract obtained from Uncaria tomentosa, the extract being derived from the inner bark or root tissue of Uncaria tomentosa.

4. The pharmacological agent of claim 2 wherein the therapeutically effective amount of Uncaria tomentosa is obtained from a commercially available source.

5. The pharmacological agent of claim 4 wherein commercially available source of Uncaria tomentosa is selected from the group consisting of pills, tablets, caplets, soft and hard gelatin capsules, lozenges, sachets, cachets, vegicaps, liquid drops, elixers, suspensions, emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged powders, bark bundles or bark powder.

6. The pharmacological agent of claim 3 wherein the extract of Uncaria tomentosa comprises an amyloid inhibitory ingredient selected from the group consisting of oxindole alkaloids, quinovic acid glycosides, proanthocyanidins, polyphenols, triterpines, plants sterols, beta-sitosterol, stigmasterol, campesterol, phytosterols, 3-beta, 6beta, 19alpha-trihydroxy-urs-12-en-28-oic-acid, 5alpha-carboxystrictosidine, alloisopteropodine, allopteropodine, angustine, dihydrocorynantheine, dihydrocorynantheine-n-oxide, hirsutine, hirsutine-n-oxide, isomitraphylline, isopteropodine, isorhynchophylline, isorhynchophylline-n-oxide, isorotundifoline, curculogoside, curculigoside B, phenolglucosides, 2-[[2,6-dimethoxybenzoyl)oxy]methyl-4-hydroxyphenyl-beta-D-glucopyranoside,2-[[2-hydroxy-6-methoxybenzoyl)oxy]methyl-4-hydroxyphenyl-beta-D-glucopyranoside, mitraphylline, oleanolic-acid, pteropodine, quinovic-acid-3beta-o-(Beta-dglucopyranosyl-(1-->3)beta-d-fucopyranosyl-(27-->1)-beta-d-glucopyranosyl-ester, quinovic-acid-3beta-o-beta-d-fucopyranoside, quinovic-acid-3beta-o-beta-d-fucopyranosyl-(27-->1)-beta-d-glucopyranosylester, quinovic-acid-3beta-o-beta-d-quinovopyranoside, rhynchophylline, rotundifoline, speciophylline, uncarine, uncarine-f, ursolic acid, cepharanthine (bisbenzylisochinoline alkaloid), berbamine (bisbenzylisochinoline alkaloid), matrine (lupine alkaloid), pilocarpine (imidazole alkaloid),

2,3-Dihydroxybenzoic acid, ferulic acid, anethole, cleistanthine (lignane), phenolglucosides, urunshiole, alpha-tocopherole (vitamin E), ubichone, maesanine, zexbrevine A/B, 12-O-tetradeoanoyl-phorbol-13-acetate, TPA (tetracyclic diterpene), saponine with aglycone oleonic acid (pentacyclic triterpene), and cynonchoside.

7. The pharmacological agent of claim 2 wherein the therapeutically effective amount of Uncaria tomentosa comprises a dosage in the range of from about 10 to 1,000 mg/kg of body weight of the patient.

8. The pharmacological agent of claim 7 wherein the therapeutically effective amount of Uncaria tomentosa comprises a dosage in the range of from about 10 to 100 mg/kg of body weight of the patient.

9. The pharmacological agent of claim 1 wherein said amyloid disease for treatment is selected from the group consisting of the amyloid associated with Alzheimer's disease, Down's syndrome and hereditary cerebral hemorrhage with amyloidosis of the Dutch type (wherein the specific amyloid is referred to as beta-amyloid protein or Aß), the amyloid associated with chronic inflammation, ~~various forms of~~ malignancy and Familial Mediterranean Fever (wherein the specific amyloid is referred to as AA amyloid or inflammation-associated amyloidosis), the amyloid associated with multiple myeloma and other B-cell dyscrasias (wherein the specific amyloid is referred to as AL amyloid), the amyloid associated with type II diabetes (wherein the specific amyloid is referred to as amylin or islet amyloid), the amyloid associated with the prion diseases including Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, kuru and animal scrapie (wherein the specific amyloid is referred to as PrP amyloid), the amyloid associated with long-term hemodialysis and carpal tunnel syndrome (wherein the specific amyloid is referred to as $beta_2$-microglobulin amyloid), the amyloid associated with senile cardiac amyloid and Familial Amyloidotic Polyneuropathy (wherein the specific amyloid is referred to as transthyretin or prealbumin), and the amyloid associated with endocrine tumors such as medullary carcinoma of the thyroid (wherein the specific amyloid is referred to as variants of procalcitonin).

10. The pharmacological agent of claim 9 wherein said amyloid disease for treatment is Alzheimer's Disease.

11. The pharmaceutical agent of claim 3 wherein the weight percentage of plant extract in the agent is in the range of from about 70% to about 95%.

12. The pharmaceutical agent of claim 1 further comprising a pharmaceutically acceptable carrier, diluent or excipient.

13. The pharmaceutical agent of claim 2 wherein the therapeutically effective amount of plant matter has an amyloid inhibitory activity or efficacy greater than 50%.

14. A method for isolating amyloid inhibitory constituents within Uncaria tomentosa plant matter, the method comprising the following steps: a) extracting the plant matter with an organic solvent, b) concentrating the extract, c) removing insoluble materials, d) precipitating amyloid inhibitory constituents with organic solvent e) recovering and redissolving the amyloid inhibitory constituents obtained in organic solvent, and f) injecting and separation by HPLC.

15. The method of claim 14 wherein the plant matter is comprised of commercially obtained pills, tablets, caplets, soft and hard gelatin capsules, lozenges, sachets, cachets, vegicaps, liquid drops, elixers, suspensions, emulsions, solutions, syrups, tea bags, aerosols (as a solid or in a liquid medium), suppositories, sterile injectable solutions, sterile packaged powders, bark bundles and/or bark powder, which contain Uncaria tomentosa, extracts or derivatives thereof.

16. The method of claim 14 wherein the plant matter is taken from commercially available gelatin-coated capsules which contain dried-powder of Uncaria tomentosa, extracts or derivatives thereof.

17. The method of claim 14 wherein the step of extracting the plant matter with an organic solvent further comprises adding propanol initially to plant materials that are powdered, and the resulting mixture is stirred overnight.

18. The method of claim 17 wherein the solvent used in the step of extracting amyloid inhibitory ingredients has a polarity ranging from that of water to that of pentanol.

19. The method of claim 14 wherein the step of removing insoluble materials is effected by centrifuging the extract and collecting the supernatant.

20. The method of claim 14 wherein the step of concentrating the extract is effected by rotary evaporation.

21. The method of claim 14 wherein following the extraction and centrifugation steps, the extraction and centrifugation procedure is repeated 5 more times and the supernatants are collected.

22. The method of claim 21 wherein following the repeated steps of extraction and concentration, the supernatants are pooled and concentrated using a rotary evaporator.

23. The method of claim 14 wherein following the concentrating step, and after the volume is about 500 mls or less, the extract is recentrifuged to further remove insoluble materials.

24. The method of claim 23 wherein following the recentrifugation step, the supernatant is obtained and precipitated with 4 volumes of petroleum ether.

25. The method of claim 24 wherein following precipitation with petroleum ether, the precipitate is collected in a pellet following further centrifugation.

26. The method of claim 25 wherein the pellet is dissolved in propanol and applied to a silica column equilibrated with propanol containing acetic acid.

27. The method of claim 26 wherein following the application of the material to a silica column, propanol containing acetic acid is used to elute, and the fastest moving yellowish-brown colored fractions are collected with a fraction collector.

28. The method of claim 27 wherein the eluents from the column are monitored spectroscopically at 490nm and fractions are collected in a fraction collector.

29. The method of claim 27 wherein following collection of the fastest moving yellowish-brown colored fractions, the fractions are precipitated with petroleum ether, and the precipitate is collected following centrifugation.

30. The method of claim 29 wherein following reprecipitation and recentrifugation, the pellet is dissolved in acetonitrile/acetic acid/water for high pressure liquid chromatography (HPLC) injection.

31. The method of claim 30 wherein the dissolved pellet is divided into equal portions and injected into an HPLC.

32. The method of claim 31 wherein the HPLC used contains a 1 X 25 cm C_{18} column, and is maintained at 30°C with a flow rate of 2 ml/min.

33. The method of claim 31 wherein sample portions injected onto the HPLC are eluted with gradients of A and B, such that 0% B for 5 minutes, 0-15% B from 5-10 minutes, 15-45% B from 10-70 minutes, and 45-100% B from 70-85 minutes; where B=95% acetonitrile with 0.5% acetic acid in distilled water and A=5% acetonitrile with 0.5% acetic acid in distilled water.

34. The method of claim 33 wherein the eluents from the HPLC are monitored at 490nm and 4 ml fractions are collected in a fraction collector and pooled peaks are obtained at various retention times (from 0 through 85 minutes).

35. The method of claim 34 wherein the fractions obtained are concentrated by lyophilization after most of the acetonitrile is removed by rotary evaporation.

36. The method of claim 35 wherein the concentrated fractions obtained are tested in relevant in vitro assays to identify inhibitors of amyloid fibril formation, amyloid fibril growth or agents which cause dissolution/disruption of pre-formed amyloid fibrils.

37. The method of claim 14 wherein the amyloid inhibitory ingredients within Uncaria tomentosa are identified to be contained within approximate HPLC retention times of 13-45 minutes.

38. The method of claim 37 wherein the amyloid inhibitory ingredients within Uncaria tomentosa are identified to be contained with an approximate HPLC retention time of 26 minutes.

39. A method of treating an amyloid disease in a patient, comprising the step of administering to the patient a therapeutically effective amount of plant matter from a plant of the genus Uncaria, species tomentosa.

40. The method of claim 39 wherein the therapeutically effective amount of plant matter comprises an amyloid inhibitory ingredient selected from the group consisting of oxindole alkaloids, quinovic acid glycosides, proanthocyanidins, polyphenols, triterpines, plants sterols, beta-sitosterol, stigmasterol, campesterol, phytosterols, 3-beta, 6beta, 19alpha-trihydroxy-urs-12-en-28-oic-acid, 5alpha-carboxystrictosidine, alloisopteropodine, allopteropodine, angustine, dihydrocorynantheine, dihydrocorynantheine-n-oxide, hirsutine, hirsutine-n-oxide, isomitraphylline, isopteropodine, isorhynchophylline, isorhynchophylline-n-oxide, isorotundifoline, curculogoside, curculigoside B, phenolglucosides, 2-[[2,6-dimethoxybenzoyl)oxy]methyl-4-hydroxyphenyl-beta-D-glucopyranoside,2-[[2-hydroxy-6-methoxybenzoyl)oxy]methyl-4-hydroxyphenyl-beta-D-glucopyranoside, mitraphylline, oleanolic-acid, pteropodine, quinovic-acid-3beta-o-(Beta-dglucopyranosyl-(1-->3)beta-d-fucopyranosyl-(27-->1)-beta-d-glucopyranosyl-ester, quinovic-acid-3beta-o-beta-d-fucopyranoside, quinovic-acid-3beta-o-beta-d-fucopyranosyl-(27-->1)-beta-d-glucopyranosylester, quinovic-acid-3beta-o-beta-d-quinovopyranoside, rhynchophylline, rotundifoline, speciophylline, uncarine, uncarine-f, ursolic acid, cepharanthine (bisbenzylisochinoline alkaloid), berbamine (bisbenzylisochinoline alkaloid), matrine (lupine alkaloid), pilocarpine (imidazole alkaloid), 2,3-Dihydroxybenzoic acid, ferulic acid, anethole, cleistanthine (lignane), phenolglucosides, urunshiole, alpha-tocopherole (vitamin E), ubichone, maesanine, zexbrevine A/B, 12-O-tetradeoanoyl-phorbol-13-acetate, TPA (tetracyclic diterpene), saponine with aglycone oleonic acid (pentacyclic triterpene), and cynonchoside.

41. The method claim 39 wherein the therapeutically effective amount of Uncaria tomentosa is administered orally.

42. The method claim 39 wherein the therapeutically effective amount of Uncaria tomentosa is administered by aerosol spray.

43. The method claim 39 wherein the therapeutically effective amount of Uncaria tomentosa is administered in a parenterally injectable or infusible form.

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